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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LAM, ANN Y	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/807,345	ARKHAMMAR ET AL.	
	Examiner	Art Unit	
	Ann Y. Lam	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 13-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 13-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/14/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Information Disclosure Statement

The information disclosure statement filed January 14, 2004 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. (Examiner is unable to locate the non-patent literature disclosed in the IDS and thus is unable to consider those publications. Examiner requests that Applicant submit or re-submit the publications if Applicant would like Examiner to consider them. In the case of resubmission, Examiner apologizes for any inconvenience.)

Claim Objections

1. Claims 21-22 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 1, lines 11-14, already recites these limitations.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-11 and 13-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1, lines 5-14, both recite the limitation "detecting translocation of light emitted from said fluorophore.....said translocation is from cytoplasm to membrane, from membrane to cytoplasm, from an aggregated form to a dispersed form or from a dispersed form to an aggregated form". Claim 31, lines 10-13, also claims the same limitation.

The specification as originally filed does not mention the step of detecting "from an aggregated form to a dispersed form or from a dispersed form to an aggregated form".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-11, 13-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, lines 2-4, and claim 31, lines 2-3, both recite the limitation "a component fused to a fluorophore in a cell in mechanically intact or permeabilised living cells". It is unclear as to what Applicant is claiming, since the claims appear to be claiming that the component is in a cell that is in cells, which does not make sense.

Claim 1, lines 5-14, both recite the limitation "detecting translocation of light emitted from said fluorophore.....said translocation is from cytoplasm to membrane, from membrane to cytoplasm, from an aggregated form to a dispersed form or from a dispersed form to an aggregated form". Claim 31, lines 10-13, also claims the same limitation. It is unclear as to what Applicant is claiming since it appears that Applicant is claiming that the emitted light changes from an aggregated form to a dispersed form, whereas Applicant's specification describes that it is the luminophore that undergoes redistribution (page 10, lines 26-28) and the intensity of the emitted light (or polarisation or wavelength shift, etc.) is measured and used to detect underlying cellular phenomena (page 10, lines 10-13).

Claim 6, line 2, recites the limitation "the spatial limitations." There is insufficient antecedent basis for this limitation in the claim.

Claim 20 does not include a transitional phrase such as "comprising", and thus it is unclear what is included in the body of the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1-5, 8-11, 13-15, 17, 18, 20-23, 26, 27 and 31 are rejected under 35 U.S.C. 102(e) as being anticipated by Miesenbock et al., 6,670,449.

As to claims 1, 21, 22, 31, Miesenbock discloses a method for detecting translocation of a component fused to a luminophore (green fluorescent protein, column 4, lines 6-62, and column 14, lines 37) in a cell in mechanically intact or permeabilized living cells (column 5, lines 29-30), the method comprising detecting translocaton of light emitted from said luminophore (column 3, lines 53-56), said translocation is detected by measuring changes in luminescence intensity (column 14, lines 6-8, 14-18, lines 26-29), said luminophore is encoded by and expressed from a nucleic acid sequence in said cell (column 5, lines 7-9, lines 14-26), and said translocation is from cytoplasm to membrane (column 18, lines 36-37), from membrane to cytoplasm, from an aggregated form to a dispersed form (column 18, lines 36-37) or from a dispersed form to an aggregated form.

As to claim 2, the translocation is caused by an influence (column 5, lines 38-41; and column 18, lines 8-10).

As to claim 3, the influence comprises contact between the mechanically intact or permeabilised living cells and a chemical substance and/or incubation of the cells with a chemical substance (column 5, lines 38-41; and column 18, lines 8-10.)

As to claim 4, the cells comprise a group of cells contained within a spatial limitation type (column 5, lines 36-41.)

As to claim 5, the cells comprises multiple groups of cells contained within multiple spatial limitations (column 5, lines 36-41.)

As to claim 8, the translocation results in quenching of fluorescence, the quenching being measure as a decrease in the intensity of the fluorescence (column 18, line 13.)

As to claim 9, the translocation results in energy transfer, the energy transfer being measure as a change in the intensity of the luminescence (column 14, lines 14-18, and 25-30; and column 18, lines 35-37.)

As to claim 10, the intensity of the light is a function of the luminescence lifetime, polarization, wavelength shift, or other property which is modulated as a result of the underlying cellular response, (column 18, lines 10-14.)

As to claim 11, the light to be measured passes through a filter which selects the desired component of the light to be measured and rejects other components (column 32, lines 22-23, column 33, line 8.)

As to claims 13, 26, the luminophore is a luminescent or fluorescent polypeptide (column 4, lines 61-62.)

As to claims 15, 27, the cells are selected from the group consisting of fungal cells, invertebrate cells, vertebrate cells (column 5, line 49.)

As to claim 14, the fluorescence comes from a fluorophore encoded by and expressed from a nucleotide sequence harboured in the cells (column 11, lines 49-50, column 12, lines 36-47.)

As to claim 17, the method is used as a screening program (column 18, lines 8-17.)

As to claim 18, the method is for screening program for the identification of a biologically active substance that directly or indirectly affects an intracellular signaling pathway and is potentially useful as a medicament, wherein the result of the individual measurement of each substance being screened which indicates its potential biological activity is based on measurement of the redistribution of spatially resolved luminescence in living cells and which undergoes a change in distribution upon activation of an intracellular signaling pathway (column 18, lines 8-17.)

As to claim 20, a set of data obtained by the above method is disclosed (column 18, lines 8-17.)

As to claim 23, the fluorescent polypeptide is a Green Fluorescent Protein (column 4, lines 61-62.)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 16,19, 24-25 and 28-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miesenbock et al., 6,670,449.

Miesenbock discloses the invention substantially as claimed (see above), except for the step of incubation at a temperature as claimed, and for the identification of a toxic substance that exerts its toxic effect by interfering with an intracellular signaling pathway, and for the specific mutant GFP claimed.

As to claims 16 and 28-30, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233. The step of incubation at a temperature that would provide an optimum result requires only routine skill in the art.

As to claim 19, Miesenbock discloses use of the method to determine the effects of drugs on exocytotic process for example (column 18, lines 9-10) and that the method can be used for screening for compounds affecting trafficking processes of medical relevance (column 18, lines 30-31.) Application of the method to discover toxic

substances that exerts its toxic effect by interfering with an intracellular signaling pathway is of medical relevance and thus such variation in the Miesenbock method would be obvious to one of ordinary skill in the art.

As to claims 24-25, Miesenbock discloses that the invention also includes mutants of green fluorescent protein which exhibit environment sensitive excitation and/or emission spectra and are useful, for example, as reporter moieties in the hybrid molecules of the invention (column 4, lines 61-65.) It would have been obvious to provide mutations of the green fluorescent protein as claimed by Applicants, as mutants of green fluorescent protein which exhibit environment sensitive excitation and/or emission spectra and are useful as reporter moieties in the invention, as taught by Miesenbock.

6. Claims 6 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miesenbock et al., 6,670,449, in view of Zarling et al., 5,674,698.

Miesenbock discloses the invention substantially as claimed (see above), except for the spatial limitations being arranged in one or more arrays on a common carrier type, and for the spatial limitations beings wells in a plate of micro-titer type.

Zarling also discloses a method for detecting intensity of light emitted from labels provided in intact viable cells (column 5, lines 9-14; and column 5, lines 66 – column 6, line 1).

As to claim 6, Zarling further discloses that the cells are contained within spatial limitations that are arranged in one or more arrays on a common carrier type (see column 39, lines 10-32.)

As to claim 7, the spatial limitations are wells in a plate of micro-titer type (see column 39, lines 10-32.)

It would have been obvious to provide in the Miesenbock method an array of wells in a plate of micro-titer type as taught by Zarling as a known mechanism used to contain cells in an assay.

Response to Arguments

Applicant's arguments with respect to the above rejected claims have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on M-Sat 11-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A.L.

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SUPERVISORY PATENT EXAMINER
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04/05/04